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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/471,749	12/23/99	HILLMAN J	PF-0519-1DIV

HM12/1218

INCYTE PHARMACEUTICALS INC
PATENT DEPARTMENT
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EXAMINER	
HARRIS, A	
ART UNIT	**PAPER NUMBER**
1642	9

DATE MAILED: 12/18/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/471,749	Applicant(s) Hillman et al.
	Examiner Alana M. Harris, Ph. D.	Group Art Unit 1642

☒ Responsive to communication(s) filed on *September 25, 2000.*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *3, 6, 7, 9-12, and 19-40* is/are pending in the applicat

Of the above, claim(s) *3, 6, 7, 9-12, 19, 20, 23-26, and 29-40* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *21, 22, 27, and 28* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. Claims 3, 6, 7, 9-12 and 19-42 are pending.

Claims 41 and 42 have been added.

Claims 21, 27, 28, 31 and 34 have been amended.

Claims 3, 6, 7, 9-12, 19-20, 23-26 and 29-42, drawn to non-elected inventions are withdrawn from examination.

Claims 21, 22, 27 and 28 are examined on the merits.

Priority

2. The Examiner acknowledges that this application now contains the necessary reference to the prior divisional application, Serial No. 09/078,402, filed May 13, 1998 following the title of the invention.

3. The Examiner has reviewed U.S. Application Serial No. 09/078,402 filed May 13, 1998 from which priority is claimed under 35 U.S.C. § 120. Claims 21, 22, 27 and 28 will be granted the May 13, 1998 priority date.

Information Disclosure Statement

4. Applicant notified the Office in the Information Disclosure Citation (Paper No. 2, filed March 10, 2000) that listed documents to be considered were originally filed in parent case #09/078,402, filed May 13, 1998. Parent case #09/078,402 was reviewed by the Examiner and the twenty-nine references listed on the IDS, Paper no. 2 were not seen in the file. Applicant is invited to provide replacement copies of listed references for consideration.

Drawings

5. The Examiner acknowledges Applicants submission of amended drawings and they have been approved by the draftsman.

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections

Claim Rejections - 35 U.S.C. § 112

7. The rejection of claims 21, 22, 27 and 28 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn in view of Applicants' arguments and amendment to claim 27.

Claim Rejections - 35 U.S.C. § 102

8. The rejection of claims 21 and 27 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent #5,925,733 (filed June 11, 1996) is withdrawn in view of Applicants' arguments.

9. The rejection of claim 21 under U.S.C. 102(b) as being anticipated by Accession #A42445 (March 3, 1993) is withdrawn in view of Applicants' argument and amendment to the claim.

Maintained Rejections

Claim Rejections - 35 U.S.C. § 112

10. The rejection of claims 21, 22, 27 and 28 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained. The reasons for this rejection are of record in paper no.8, mailed June 20, 2000.

11. Claims 21, 22, 27 and 28 remain rejected under 35 U.S.C. 112, first paragraph is maintained. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth below, one skilled in the art clearly would not know how to use the claimed invention. The reasons for this rejection are of record in paper no. 8, mailed June 20, 2000.

Claim Rejections - 35 U.S.C. § 101

12. The rejection of claims 21, 22, 27 and 28 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility is maintained.

The Applicants argue that "The rejection of claims 21, 22, 27 and 28 is improper...," and as claimed "the claimed invention has numerous practical, beneficial uses in toxicologic testing, drug development and the diagnosis of diseases, none which necessarily require detailed knowledge of how the polypeptide coded for by the polynucleotide works." This is not found persuasive. There is no objective evidence of record to show that the HAPOP-1, 2, 3 or 4 molecules can be used in the treatment of cell proliferative disorders and a host of other disorders affecting immunocompromised individual. The data provided by Applicants suggest a correlation between the expression of the claimed sequences in various libraries. The mere expression in a tissue does not mean treatment.

Applicant argue that in view of the above arguments, the claimed invention has utility. Applicant has not correlated the claimed polypeptides, SEQ ID NO:3 or 5 to any such use. As stated in Brenner v. Manson (383 U.S. 519, 535-536, 148 USPQ 689, 693, 696 (1966)) "[i]t was never intended that a patent be granted upon a product..unless such product be useful" and "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". Applicants in their specification are merely "hunting" and has not provided any successful conclusion.

Applicant argues that they have established a "well-established" utility. Since there is no correlation between the claimed products and a specific use, the Examiner disagrees.

Applicants argue that the genes are tools used in expression profiling (see page 12 of response). "Tools" are merely used to "hunt" with and do not provide any successful conclusion.

Applicants argue that the claimed invention is known to be useful because whole classes of genes are routinely incorporated for use in toxicology testing and expression profiling. Expression profiling is used to identify drug targets and characterize disease. While that is true what are the conditions caused by theses human apoptosis associated proteins? If applicant cannot demonstrate any objective evidence to show that HAPOP-1, HAPOP-2, HAPOP-3 and HAPOP-4 causes any conditions, then one skilled in the art would not only have to see which drugs can change the activity of these proteins but also would have to determine the condition. And clearly undue experimentation would be required to do this.

Applicants argue that just because the invention belongs to a broad class that does not negate its utility. The Examiner never said it did. In fact, the Examiner is looking at the specific protein and its relationship to other known proteins. While the PTO does issue patents to broad classes there is well-established, substantial and specific utility for those broad classes.

Additionally, the Applicants argue that the claimed invention's uses as a tool for toxicology testing is a practical and real-world use, hence it is a "substantial" use. There is no objective evidence of record to show that this claimed novel proteins can be used to treat cell proliferative disorders such as sarcomas, cancers of the cervix, ganglia and testis. Furthermore, characterizations based on structural/functional relationships have many problems. Bork

(Genome Research 10:398-400, 2000) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, col 3). Furthermore, recent studies show that alternative splicing might affect more than 30% of human genes and the number of known post-translational modifications of gene products is increasing constantly so that complexity at protein level is enormous. Each of these modifications may change the function of respective gene products drastically (p. 399, col 1). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, col 2). Most features predicted with an accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399 para bridging cols 2 and 3). The reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those feature are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, para bridging cols 1 and 2).

Applicant argues that requiring applicant to state a particular utility misstates the law. The Examiner never required applicant to state such--applicant stated the utility in the specification and the Examiner is asking for objective evidence to support this.

Claim Rejections - 35 U.S.C. § 102

13. The rejection of claims 21 and 27 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent #5,919,660 (filed June 24, 1997) is maintained. Applicants strenuously object to the applied 102 rejection on the basis it is scientifically incorrect and that is an unsupported assertion that such a fragment be considered biologically active by one skilled in the art. This is found unpersuasive.

Sequence 2 of U.S. Patent # 5,919,660 (see column 41) continues to disclose a substantially purified polypeptide comprising amino acid residues # 315-320 which corresponds with amino acids # 319-324 of SEQ ID NO:5. This is a biologically-active fragment of the amino acid SEQ ID NO:5 having apoptotic activity as referenced in column 1, lines 55-58, the same as that claimed. Also disclosed is a pharmaceutical composition comprising an effective amount of a polypeptide of claim 21 and a pharmaceutically acceptable excipient (claim 27), see bridging paragraph of columns 29 and 30, lines 41-65.

14. The rejection of claim 21 under 35 U.S.C. 102(b) as being anticipated Accession # A55302 (July 8, 1995) or Gabig et al. (J. Biol. Chem. 269:29515-29519, 1994) is maintained. Applicants' argument has been discussed above. The argument has been found unpersuasive.

Accession # A55302 or Gabig (see page 29517, Fig. 4) continue to disclose a substantially purified polypeptide comprising amino acids # 281-287 of attached amino acid database sheet which corresponds with amino acids # 319-325 of SEQ ID NO:5. This would be biologically-active fragment of SEQ ID NO:5 having apoptotic activity, the same as that claimed (see abstract of Gabig, last sentence).

New Rejections

Claim Rejections - 35 U.S.C. § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 21 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Accession # A55302 (July 8, 1995) or Gabig et al. (J. Biol. Chem. 269:29515-29519, 1994), in view of Harlow and Lane (Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory, 1988). The teachings of the aforementioned references have been discussed above. Accession # A55302 (July 8, 1995) or Gabig et al. (J. Biol. Chem. 269:29515-29519, 1994) do not teach the polypeptides comprised in a composition such as an adjuvant contained with saline, mineral oil or aluminum hydroxide.

Harlow and Lane teach the pharmaceutically acceptable diluent of pH neutral, phosphate buffered saline solution for the storage of polypeptides and the production of adjuvants. It would

have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to formulate a pharmaceutical composition comprising a carrier/excipient and the polypeptides of claim 21 in order to store the polypeptides in solution for the purpose of making an adjuvant. One of ordinary skill in the art would have been motivated to store the polypeptides in saline because Harlow and Lane teach that these components are necessary when producing an effective adjuvant. Moreover, one of ordinary skill in the art would have had a reasonable expectation of success in placing the polypeptides of claim 21 in a pharmaceutically acceptable carrier such as saline because this protocol is a standardly used immunological technique described in basic antibodies manual such as Harlow and Lane.

Because pharmaceutically acceptable carriers such as sterile saline solution and phosphate-buffered-saline solution were well known in the art, one of ordinary skill in the art at the time of the claimed invention would have known how to formulate a pharmaceutical composition comprising a carrier/excipient and the instantly claimed polypeptides.

When the claim is directed to a product, the preamble or intended use is generally nonlimiting if the body of the claim is directed to an old composition and the preamble merely recites a property inherent in the old composition. [*Kropa v. Robie*, 88 USPQ 478, 480-81 (CCPA 1951); see also MPEP 2111.02]. Thus, art which reads on a compound may also be applied to pharmaceutical compositions consisting essentially of said compound and a suitable pharmaceutical carrier.

It has been held by the Court that a compound and a carrier are obvious, if it is obvious in the art to utilize a carrier with related compounds. See In re Rosicky, 125 USPQ 341 (CCPA 1960).

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris whose telephone number is (703)306-5880. The examiner can normally be reached on Monday through Friday from 6:30 am to 3:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703)308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703)308-0196.

Alana M. Harris, Ph.D.
Patent Examiner, Group 1642
December 14, 2000

SHEELA HUFF
PRIMARY EXAMINER